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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,274	THOMAS ET AL.	
	Examiner	Art Unit	
	Medina A Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,22-24,28-31 and 33-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 22-24, 28-31 and 33-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). ____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's response filed 12/11/03 in reply to the Office action mailed 07/31/03 has been entered. Claims 5-21, 25-27, 30 and 32 have been cancelled. Claims 33-38 have been added. Therefore, claims 1-4, 22-24, 28-31 and 33-38 are pending and are under consideration.

This Office action contains NEW GROUNDS OF REJECTIONS not necessitated by Applicant's amendments. Therefore, this action is non-final. The delay in applying these grounds of rejection is regretted.

All previous rejections and objections not set forth below have been withdrawn in view of Applicant's amendment.

Priority

Applicant has not complied with the conditions for receiving benefit of the foreign filing date because a certified copy of the foreign priority application as required by 35 U.S.C. 119(b) has not been submitted. Applicant is required to provide the certified copy of the foreign priority in order to receive the foreign filing date, as stated in the last Office action.

Claim Rejections - 35 USC § 112

Claims 1-4, 7-9 and 27-29, 31 remain rejected and new claims 33 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing necrotic effect in specific cells of a plant by

expressing pokeweed antiviral protein (PAP) encoding sequences of SEQ ID NO: 1, 3, 5, or 7 in said cells and plants and plant cells produced by said method, does not reasonably provide enablement for a method that employs any part of the coding sequence of a mature PAP, a coding sequence that is 70% homologous to SEQ ID NO: 3, 5, or 7 and having the same functionality thereof, a sequence encoding a sequence having at least 80% homologous to SEQ ID NO: 4, 6, or 8 and having the same functionality. This rejection is repeated for the reasons of record as set forth in the last Office action of 07/31/03. Applicant's arguments filed 11/25/03 have been considered but are not deemed persuasive.

Applicant argues that the instant application provides ample guidance for one skilled in the art to practice the claimed invention without undue experimentation. Applicant relies the following points to support this position: firstly, Applicant argues that the specification teaches domains of PAP sequences including PAP-S α and PAP-Sβ that are critical for PAP function are disclosed in the specification. Secondly, the techniques for plant transformation, the skills to determine which parts and homologous sequences of the disclosed sequences would retain the desired function, and exposing the transformed plant to a pathogen or a chemical or stimulating the natural development of said plant are well within the level of one of skill known in the art. Thirdly, the working examples disclosed in the specification include the use of mature PAP-S, PAP-S α and β that are homologous to the pro-PAP sequence from which they are derived; and PAP-Sα and PAP-Sβ that are homologous and parts of the mature-PAP-S. Applicant, therefore, asserts that one skilled in the art who follows the direction

and guidance outlined in the specification would be able to make the nucleotide sequences as broadly claimed, and use them to induce necrotic effect in a transgenic plant, without undue experimentation. Applicant cites case laws to support the conclusion.

These arguments are not persuasive because the claimed method of inducing necrotic effect in a transgenic plant by expressing any nucleotide sequence encoding "a part" of mature PAP, or any sequence that is 70% and 80% homologous to the disclosed sequences and capable of inducing necrotic effects, constructs comprising said nucleotide sequence and plants produced by said method are not supported by enabling disclosure. The specification does not provide guidance other than the use of nucleotide sequences SEQ ID NO: 1, 3, 5, and 7 encoding SEQ ID NO: 2, 4, 6, and 8, respectively.

In Genentech Inc v. Novo Nordisk A/S (42 USPQ2d 1001 at p. 1005). The CAFC stated, "(P)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable....While every aspect of generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention...". . See also *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it states " the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. In the instant application, the nucleotide sequences encoding "a part" of mature PAP and homologous sequences of the claimed method encompass

fragments of any size of SEQ ID NO: 1-2, 3-4, 5-6 and 7-8 and modified sequences thereof having multiple deletions and substitutions that retain PAP activity. However, Applicant has not provided guidance with respect to modifications of the disclosed sequences, other than N-terminal and C-terminal deletions of the Pro- PAP-S, and the PAP-S α and PAP-Sβ domains of the mature PAP-S having PAP activity. On page 46 of Applicant's own specification, results show that the transformation of tobacco with the mature PAP-S sequence failed to produce the desired transgenic plant. Therefore, it is unpredictable whether transformation of any plant with any part of a mature PAP, or any sequence that is 70% and 80% homologous to the disclosed sequences would actually yield plants having the desired phenotype, necrosis in specific cells. Note, methods that employ nucleotide sequences encoding pro-PAP (SEQ ID NO: 2), mature PAP-S (SEQ ID NO: 4), PAP-S α (SEQ ID NO: 6) and PAP-Sβ (SEQ ID NO:8) and transgenic plants produced by said methods, and chimeric genes comprising said nucleotides are not included in the rejection.

Therefore, for the reasons discussed above and in the last Office actions, the claimed invention is not enabled throughout the broad scope. Therefore, the rejection is maintained.

Written Description

Claims 1-4, 7-9 and 27-29, 31 remain rejected and new claims 33 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. This rejection is repeated for the reasons of record as set forth in the last Office action of 07/31/03. Applicant's arguments filed 11/25/03 have been considered but are not deemed persuasive.

Applicant argues that the claimed invention are adequately described and meet the requirement of written description. Applicant relies the following points to support this position: a representative examples of PAP encoding sequences that induce necrotic effect has been disclosed in the specification; several PAP sequences are known in the art; and the level of skill in the art is high.

This is not persuasive because a representative number of nucleic acid sequences having at least 70%, 80% homology to the disclosed sequence and having the same functionality, and a method that employs therewith to induce necrotic effect in a plant have not been described. While the specification describes methods that employ nucleotide sequences encoding pro-PAP (SEQ ID NO: 2), mature PAP-S (SEQ ID NO: 4), PAP-S α (SEQ ID NO: 6) and PAP-Sβ (SEQ ID NO:8) and transgenic plants produced by said methods, and chimeric genes comprising said nucleotide sequences; the claimed invention is not limited to the use of PAP sequences but encompass non-PAP sequences that induce necrotic effect which Applicant clearly was not in possession at the time of filing. Note the claims do not read the homologous sequence has PAP-S activity. Therefore, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that one skilled in the art would recognize that Applicants are in possession of the invention as broadly claimed, as stated in the last Office action. The rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 1-4, 22- 24, 28-29, 31 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanieswski et al (6, 015, 940) in view of Baszczynski et al (5,756, 324).

Kanieswski et al teach a method of inducing viral resistance in tobacco and potato plants and plant cells, the method comprising transforming said plants/plant cells with a chimeric gene comprising a DNA sequence encoding PAP or a mutant thereof retaining PAP activity, a tissue-specific or inducible promoter, N-terminal signal sequence capable of targeting said PAP' in specific cells of the plant. The reference further teaches transgenic potato plants that are resistant to PVX, PVY and PLRV (potato virus X, Y, and potato leaf roll viruses) (column 2; column 9, lines 24-41; Examples 2-3; and columns 27-28). In column 3, lines 2-10 and column 4, lines 3-30, Kanieswski suggests that other forms of PAP including PAP-S and PAP-II can be isolated from pokeweed seed and summer leaf, respectively, and used in the disclosed method. In column 9, lines 25-45, the cited reference suggests expressing the pokeweed antiviral protein in a tissue-specific manner in cells where viral infection is known to occur.

While Kanieswski et al suggest cell-specific expression of PAP, Kanieswski et al do not expressly teach cell-specific expression of PAP to induce necrotic effect.

Baszczynski et al teach expression of gene encoding pokeweed antiviral protein under the control of the microspore-specific promoter of Bnm1. The reference teaches

that the microspore-specific promoter of Bnm1 induces gene expression in the microspores of transgenic plants beginning at the uninucleate stage of development as well as in tapetal cells. (column 17, 1st full paragraph; and Example 5). Since PAPs are ribosome-inhibiting proteins and are known to inactivate plant ribosomes (see column 1, lines 44-50), the necrotic effect is expected.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of transforming a plant with a pokeweed antiviral protein encoding DNA as taught by Kanieswski et al, and to modify that method by incorporating any other PAP encoding DNA sequence with a cell-specific regulatory element to induce cell-specific necrosis. One would have a reasonable expectation of success to induce viral resistance as taught by Kanieswski et al, or necrotic effect in specific plant cells as taught by Baszczynski et al. Note, the definition of "necrotic effect" in the specification. One would have been motivated to do so because PAPs are known to induce necrotic effects as well as antiviral activity in plants (ribosome inactivating proteins). Therefore, the claimed invention as whole was clearly a *prima facie* obvious.

Applicant's argument that neither Kanieswski nor Baszczynski suggests necrotic effect by PAP is not persuasive because PAPs are known in the prior art to induce both antiviral and protein synthesis inhibiting activities in plants. Kanieswski teaches antiviral activity by PAPs in a transgenic plant, and suggest cell-specific expression of the PAP. Baszczynski teaches cell-specific expression of PAP. One of ordinary skilled in the art would have been motivated to use PAP encoding sequences to induce necrotic effect

and/or viral resistance in specific cells of a plant, with a reasonable expectation of success.

In addition, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Remarks

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM . Before and After final

responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

2/23/04
Mai

Medina A. Ibrahim